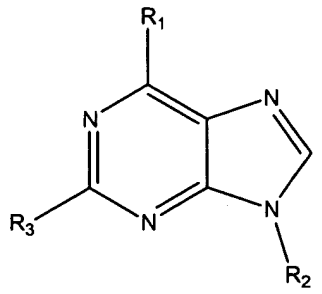
ABSTRACT OF THE DISCLOSURE

Disclosed are novel compounds that are inhibitors of CDK2 and IκB-α cell cycle kinases, useful for treating various disease states, including proliferative diseases such as cancer and restenosis.

IN THE CLAIMS:

Please enter new claims 92-114, and upon their entry cancel claims 50-88 & 91 without prejudice.

92. (New) A compound of Formula (I):



Formula (I)

wherein:

R_1 is -X-R_1'; in which R_1' is alkyl, cycloalkyl, aryl, aralkyl, hetaryl, or heterocyclyl, of which alkyl, cycloalkyl, aralkyl, hetaryl, or heterocyclyl are optionally substituted with 1-3 substituents chosen from hydroxy, halogen, trifluoromethyl, alkyl of 1-4 carbon atoms, or alkoxy of 1-4 carbon atoms, and X is -NH-;

R_2 is lower alkyl optionally substituted with one, two or three groups selected from hydroxy, lower alkoxy, and halogen; and

R_3 is $-NR_4R_5$; in which R_4 and R_5 independently are hydrogen or lower alkyl optionally substituted with one, two or three groups selected from hydroxy, lower alkoxy, halogen, amino, or carboxyl,

with the proviso that:

(1) when R_1 is benzyl or phenylethyl, X is -NH-, and R_3 is NR_4R_5, in which R_4 is hydrogen and R_5 is lower alkyl of C_{1-4} substituted by hydroxy or amino, R_2 is not methyl or ethyl;

(2) R_1 cannot be cycloalkyl or endo-2-norbornyl when R_3 is halogen, hydroxy, or alkoxy;

when R_1' is optionally substituted alkyl, the optional alkyl substitution is not heteroaryl;

(3) when R_3 is 2-hydroxyethylamino and R_2 is methyl, R_1-X is not 3-methyl-2-butenylamino, benzylamino, or m-hydroxybenzyl-amino,

(4) when R_3 is 2-hydroxyethylamino and R_2 is isopropyl, R_1-X is not benzylamino, m-hydroxybenzylamino, or 3-methylbutylamino;

(5) when R_3 is 2-hydroxyethylamino and R_2 is 2-hydroxyethyl, R_1 -X is not benzylamino and

(6) when R_3 is selected from the group consisting of 2-methyl-2-hydroxy propylamino and 2-dimethylaminoethylamino and R_2 is methyl, then R_1-X is not benzylamino;

or an acid addition salt or cationic salt thereof.

93. (New) The compound of claim 92, wherein R_1' is aralkyl, or hetaryl.

94. (New) The compound of claim 93, wherein R_4 and R_5 independently are hydrogen or lower alkyl substituted with hydroxy or amino.

95. (New) The compound of claim 94, wherein R_4 is hydrogen and R_5 is lower alkyl substituted with amino.

96. (New) The compound of claim 95, wherein R_2 is lower alkyl and R_5 is 2-aminoethyl or 2-aminopropyl.

97. (New) The compound of claim 96, wherein R_1' is benzyl optionally substituted with 1-3 substituents chosen from alkyl of 1-4 carbon atoms, alkoxy of 1-4 carbon atoms, and halogen.

98. (New) The compound of claim 97, wherein R_1' is 4-chlorobenzyl, R_2 is isopropyl, and R_5 is 2-aminoethyl; namely {2-[(2-aminoethyl)amino]-9-(methylethyl)purin-6-yl}[(4-chlorophenyl)methyl]amine (CVT-2584).

99. (New) The compound of claim 97, wherein R_1' is 4-chlorobenzyl, R_2 is isopropyl, and R_5 is 2-aminopropyl; namely {2-[(2-aminopropyl)amino]-9-(methylethyl)purin-6-yl}[(4-chlorophenyl)methyl]amine (CVT-2608).

100. (New) The compound of claim 94, wherein R_4 is hydrogen or lower alkyl substituted with hydroxy and R_5 is lower alkyl substituted with hydroxy.

101. (New) The compound of claim 100, wherein R_2 is lower alkyl and R_4 and R_5 are both 2-hydroxyethyl.

102. (New) The compound of claim 101, wherein R_1' is benzyl optionally substituted with 1-3 substituents chosen from alkyl of 1-4 carbon atoms, alkoxy of 1-4 carbon atoms, and halogen.

103. (New) The compound of claim 102, wherein R_1' is 4-chlorobenzyl and R_2 is isopropyl, namely 2-[(6-{[(4-chlorophenyl)methyl]amino}-9-(methylethyl)purin-2-yl)(2-hydroxyethyl)amino]ethan-1-ol (CVT-2454).

104. (New) The compound of claim 102, wherein R_1' is 3,5-difluorobenzyl and R_2 is isopropyl, namely 2-[(6-{[(3,5-difluorophenyl)methyl]amino}-9-(methylethyl)purin-2-yl)(2-hydroxyethyl)amino]ethan-1-ol (CVT-2849).

105. (New) The compound of claim 101, wherein R_1' is heteroaryl optionally substituted with 1-3 substituents chosen from alkyl of 1-4 carbon atoms, alkoxy of 1-4 carbon atoms, and halogen.

106. (New) The compound of claim 105, wherein R_1' is quinolin-3-yl and R_2 is isopropyl, namely 2-{(2-hydroxyethyl)[9-(methylethyl)-6-(3-quinolylamino)purin-2-yl]amino}ethan-1-ol (CVT-1899).

107. (New) The compound of claim 100, wherein R_2 is lower alkyl, R_4 is hydrogen, and R_5 is 2-(3-methylbutan-1-ol).

108. (New) The compound of claim 107, wherein R_1' is 3,5-difluorobenzyl and R_2 is isopropyl, namely 2-[(6-{[(2,5-difluorophenyl)methyl]amino}-9-(methylethyl)purin-2-yl)amino]-3-methylbutan-1-ol (CVT-2855)

109. (New) A method of inhibiting a cell cycle kinase characterized as CDK2, comprising administering to a mammal in need thereof a therapeutically effective dose of a compound of claim 92.

110. (New) The method of claim 109, wherein the inhibition of CDK-2 kinase treats a proliferative disease in which pathogenesis involves abnormal cell proliferation.

111. (New) The method of claim 110, wherein the disease state is rheumatoid arthritis, lupus, diabetes, multiple sclerosis, cancer, restenosis, host-vs-graft disease, or gout.

112. (New) The method of claim 110, wherein the proliferative disease state is cancer.

113. (New) The method of claim 110, wherein the proliferative disease state is restenosis.